#20

Patent Application
PC9824AJRJ

I hereby certify that this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Hon. Commissioner for Patents, Washington, D.C. 20231 on this 21st day of February, 2003.

By Deanna L. Miller
(Signature of person mailing)
Deanna L. Miller
(Typed or printed name of person)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: William John Curatolo, et al. :

SERIAL NO.: 09/380,885 : Examiner: S. Sharareh:

FILED: September 7, 1999 : Art Unit: 1615

FOR: Delayed-Release Dosage Forms of Sertraline :

Hon. Commissioner for Patents
Washington, D.C. 20231

Sir:

RESPONSE

This is in response to the final Office Action of September 13, 2001. A Petition for Revival of an Application for Patent Abandoned Unintentionally under 35 CFR 1.137(b), petition fee and statement that the entire delay was unintentional are attached.

Reexamination and reconsideration of this application are respectfully requested in view of the following comments.

The invention herein is directed to a delayed release oral dosage form of sertraline. That is, the dosage form has a delay period engineered into it during which it releases 10% or less of its contained sertraline, and after which it effects immediate release of its remaining sertraline. The delay minimizes gastric exposure to sertraline and, accordingly, minimizes side effects, which are partially or primarily mediated by direct contact of sertraline with the upper gastrointestinal tract, rather than being mediated systemically.

The delay can be a spatial delay, meaning that the dosage form is sensitive to its environment of use. The delay can also be temporal, meaning that the dosage form delays the release of sertraline for a set period of time, which is not related to its position along the gastrointestinal tract.

Advantageously, Applicants provide a dosage form of sertraline, which has a shorter Tmax, the time it takes for sertraline to reach its maximum value in the blood, than conventional immediate release sertraline dosage forms. This permits faster appearance of sertraline in the bloodstream, and a potentially faster therapeutic effect.

The claims have been rejected under 35 USC 103(a) as being unpatentable over Bechgaard et al. EP 0080341 in view of the teachings of Drug Facts and Comparisons. The Examiner's comments have been carefully considered, and the rejection is respectfully traversed.

A major argument put forward by the Examiner is that sertraline was known to have gastric side effects, as disclosed in Facts and Comparisons. At page 3 of the Office Action the Examiner states:

> Sertraline is clearly documented to cause gastritis and GI ulceration in up to 1% of the patients who utilize it (Facts). Further, it is conventional in the art to alleviate drug-induced gastritis of an oral compound by formulating an enteric coated form of such compound. For example, it is well known in the art that aspirin causes GI ulceration and gastritis, however, incidents of such adverse events are much reduced when an enteric coated form of aspirin is utilized. In fact, Bechgaard discusses such conventional practice in the art in his Patent...

With due respect, the Examiner has misread Facts and Comparisons. The Examiner is under the mistaken impression that Facts and Comparisons indicate sertraline causes gastritis and ulcers in up to 1% of patients. Rather, upon a closer reading of Facts and Comparisons, it may clearly be seen that the reference states sertraline causes less than 0.1% gastritis and hemorrhagic peptic ulcer, in addition

to a wide variety of unrelated side effects at <0.1% (hiccup, proctitis, gum hyperplasia, incontinence, etc.). The statement in Facts would be standardly interpreted by a skilled artisan, to whom this application is directed, as an indication that such side effects at <0.1% are indistinguishable from the incidence in the general population, and cannot be claimed to be drug related. Thus, there cannot seriously be alleged that the disclosure provides motivation to prepare a dosage form to overcome a side effect that occurs at <0.1% incidence.

Applicant submits that a more appropriate reference for showing incidence of side effects is the Physician's Desk Reference (PDR), which describes the observations in controlled clinical trials. A copy of pages 2399 - 2404 of the 2000 PDR, along with an Information Disclosure Statement and PTO Form PTO-FB-A820 are attached. In one set of clinical trials involving 1824 patients on Zoloft and 1501 patients on placebo, nausea was observed in 28% of the drug treated patients and in 13% of the placebo treated patients. For vomiting, the incidence was 4% on drug and 2% on placebo. For diarrhea/loose stools, the incidence was 20% on drug and 9% on placebo. By contrast, gastritis is listed in a section on "Other Events Observed During the Premarketing Evaluation of Zoloft (sertraline hydrochloride)." This section lists additional events observed in multidose studies of sertraline in ~3800 subjects. To be listed, the event must have occurred once during a multidose study, and the section states: "It is important to emphasize that although the events reported occurred during treatment with Zoloft, they were not necessarily caused by it." These events, which are not necessarily drug-related, are classified into groups titled "Frequent", "Infrequent" and "Rare". Gastritis and ulcer are in the "Rare" category.

Applicants maintain that contrary to the Examiner's allegations, the cited art does not provide a basis for knowing whether a delayed release dosage form will alleviate the side effects of nausea and vomiting. While the literature may be replete with generalities about alleviating side effects with controlled release dosage forms, Applicants' experience has not supported this generalization.

On page 4 of the Office Action, the Examiner states "Bechgaard suggests the use of anti-depressives as suitable active substance (page 8, line 24). Sertraline is an anti-depressive agent, therefore, there is suggestion in the art to formulate a delayed release formulation of Sertraline." Applicants have already shown by the above comments that the combination of the Bechgaard reference with Facts and Comparisons is inappropriate. Further, Applicants submit that the mere listing of a series of general therapeutic drug groups, as in Bechgaard, cannot be considered grounds for asserting that enteric dosage forms of sertraline are obvious.

Additionally, the Examiner's discussion on page 5 of the Office Action directed to sertraline sharing the same type of gastric side effects as indomethacin and acetylsalicylic acid is based on a misreading of Facts and Comparisons.

To summarize, Applicants' submit there is no way one of ordinary skill in the art would find their invention obvious from any combination of Bechgaard et al. and Facts and Comparisons. The mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 221 USPQ 1125 (Fed Cir 1984). There is no such suggestion here. Applicants' respectfully submit that the only way one of ordinary skill in the art would find their invention obvious from any combination of the references is by hindsight. And, the law is emphatic that hindsight is an improper standard. The Federal Circuit has explained the proper test:

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in light of the prior art. Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure..

In re Dow Chemical Co., 5 USPQ.2d 1529, 1531 (Fed. Cir. 1988); Amgen, Inc. V. Chugai Pharmaceutical Co. Ltd. 18 USPQ.2d 1016. 1022-23 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). Again, neither of the references, or any combination thereof, comes even close to suggesting Applicants' invention, let alone providing any expectation of success.

The Examiner is respectfully urged to reconsider the rejections in this application as it is submitted that, for the reasons stated above, they simply are not tenable and/or are otherwise based on hindsight.

Accordingly, in view of the present amendments and comments, the rejections under 35 USC 103 have been overcome. Withdrawal of such rejections is requested.

The claims have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over copending application 09/380,897. At such time there is an indication of allowable subject matter herein, Appliants will file a terminal disclaimer thus obviating the rejection.

This application is believed to be in condition for allowance. Favorable consideration is respectfully requested.

The Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§ 1.16 and 1.17, or to credit any overpayment to Deposit Account No. 16-1445.

Respectfully submitted,

Date: Feb. 21, 2003

Carmella A. O'Gorman
Attorney for Applicant(s)
Reg. No. 33,749

Pfizer Inc.
Patent Department, MS8260-1611
Eastern Point Road
Groton, CT 06340
(860) 686-1847

56074